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Vol. II **AUGUST 1946** **No. 9**

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"Application for entry as second class matter is pending"

ACUTE LEUKEMIA

Case Report No. 66

Dr. Frances Ayres M. H.—46–5190

M. H., a 5 month old white female, was admitted to this hospital on June 12, 1946 with the diagnosis of leukemia. The child had first been seen by Dr. Hood on April 4 (about 2 months ago), at the age of 3 months, because of a slight nasopharyngitis. A history taken at this time revealed that she had been a full term, 6 lb. 11 oz. baby, who had no abnormalities and who had an uneventful neonatal course. Breast feeding was discontinued after one week and she was put on an evaporated milk formula, on which she did well and gained weight. Vitamins were started at the usual time. Physical examination at this time revealed a well developed, well nourished baby who was alert and active with a lusty cry. The upper respiratory tract was clear, the heart and lungs normal, the skin clear, and there was no enlargement of the liver, spleen, or lymph nodes.

The child continued to gain weight and solid foods were gradually added to her diet. On April 20, because of a direct exposure to measles, 3 cc. of human immune globulin was given intramuscularly without any reaction.

On May 27 the baby was seen because of a swelling in the right inguinal region. Examination at this time showed that she had gained 27½ oz. since the previous check-up. A mass, 3 cm. in diameter, was found in the right inguinal region; it was somewhat egg shaped, attached to the underlying tissue, and was located below the inguinal ligament and lateral to the inguinal ring. There was no evidence of injury or infection of the right leg. The glands in the left groin were not enlarged and the rectal temperature was 100°. There was no generalized glandular swelling and the liver and spleen were not palpable.

Ten days later the child was seen again. Her mother said that she was not taking her formula quite as well as formerly and that she was constipated and somewhat more restless than usual. The baby was alert and playful and did not appear ill. The inguinal mass at this time was distinctly smaller, lobulated, and much firmer. The liver was enlarged 4–5 cm. below the costal margin and the spleen was enlarged to the level of the umbilicus. On the legs there were several bluish-red lesions, each about 3 cm. in diameter.

A blood count on this date, June 10, showed 2,980,000 red blood cells and 5.4 grams of hemoglobin. The white blood cell count was 1,400,000 with 8% polys, 12% myelocytes and 80% myeloblasts. The diagnosis was considered to be myeloblastic type of myeloid leukemia.

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Physical examination done on admission here showed essentially the same findings as described above. The blood count on entry showed the following: 1,800,000 red blood cells, hemoglobin 3.5 gms., white blood cells 454,000 and absent thrombocytes. Dr. Rice reported the smear as follows: "Approximately 2% of the leucocytes are oxidase positive. Nearly 100% are mononuclear cells. However, I am unable to definitely determine if they are members of the granulocytic or lymphocytic series. Most of these cells are blast or miniature forms. A rare cell in mitosis is noted. Numerous microcytes and marked achromia. Diagnosis: Acute leukemia."

An x-ray of the long bones and skull taken on June 14 was reported as showing no abnormality except signs of moderate osteochrondritis over the ends of the ulna and radius.

In the interests of brevity the course in the hospital and the treatment will arbitrarily be divided into three periods. The treatment consisted primarily of a copper dye preparation especially prepared by Dr. Charles S. Gischickter. For the first 9 hospital days the patient was given a total of 105 mgms. of the dye intramuscularly in daily doses of 0.2 cc. During this period the white blood cell count dropped from 650,000 to 50,000. The red-cell count and hemoglobin was maintained by 3 transfusions.

Clinically there were definite signs of improvement. The liver decreased approximately 1 cm. in size, the spleen decreased 2 cm. and the right inguinal lymph node became much smaller. However, she developed slight melena and also a left hemiparesis. Despite the fact that she maintained her weight and fluid intake, her general condition was slightly downhill.

During the following 10 days she was given no dye preparation and her white blood cell count remained below 50,000. The paresis completely disappeared but bony masses were noted on her skull and edema of the feet developed. There was no other essential change in her condition during this time.

On the 20th hospital day her white blood cell count started to rise and for this reason the dye preparation was resumed, this time in slightly larger doses. A quarter of 1 cc. was given daily for 6 days and then 1 cc. of a stronger preparation was given daily for 4 days. During the first 11 days of this period the count rose from 75,000 to 197,000, but after the larger dose of dye was given for 2 days the count in 6 days fell from 197,000 to 23,000. The liver at this time showed little change in size. The spleen, however, was barely palpable. The inguinal lymph nodes had again become large and the edema and masses on the head persisted.

During this 17 day period she developed a 3 plus generalized lymphadenopathy. At the site of injection of the copper dye she developed a pustular abscess which resolved with aspiration. A rash appeared towards the end of this period. It first was miliaria-like in character but soon

became pustular with surrounding areas of erythema. Many of these broke down and ulcerated.

Despite the many evidences of improvement the child's general condition was becoming steadily worse. She was pallid, restless and appeared acutely ill. The infant expired on July 24, forty-two days after admission.

Discussion

Charles Geschicter, M.D.:

This case, with its acute onset, high white count (over 650,000), marked anemia, fever, enlargement of the spleen, liver and lymph nodes, and subcutaneous hemorrhages, is characteristic of leukemia in children. The age of onset, 5½ months, is rather unusual, but cases have been described in the newborn.

Incidence and Varieties of Leukemia: Leukemia in children, as in adults, may be of the myelocytic, lymphocytic or monocytic variety and either acute or chronic. Over 90% of the cases occurring in children before the 8th year are acute and the majority of cases between the ages of 8 and 22 also belong to this rapidly-progressing form. After the age of 22 years, the chronic forms of leukemia predominate. Most authors regard the subacute form as a variation of acute leukemia. The distinction, at present, is entirely arbitrary. Cases with a fatal termination within a year are classed as acute; those who die after from 1 to 2 years of symptoms are classed as subacute; and those surviving 2 to 5 years are regarded as chronic.

The majority of cases of leukemia in children are myelogenous. The old opinion that lymphogenous forms predominated was due to the difficulty in recognizing the myeloblasts. It must be remembered that this primitive granulocyte which was formerly mistaken for a lymphoblast was not correctly described until 1900 by Naegeli. Chronic myelogenous leukemia has its highest incidence in adults under the age of 50 years; whereas, after 50, chronic lymphocytic leukemia is most common. In the United States, leukemia is responsible for from 3500 to 4000 deaths annually. A small percentage of chronic leukemias, treated by irradiation, may survive the 5-year period, but the disease is invariably fatal. The incidence of the disease is on the increase. This may be because of the better recognition of the sub-leukemic form. The use of the sulfonamides and irradiation in medicine, however, may play a role, since both have been proved to increase the incidence of leukemia in animals.

Symptomatology and Physical Findings: The cardinal symptoms of leukemia in children are anorexia (with nausea or vomiting), weakness and loss of weight, extreme pallor and purpuric spots. On physical examination, there is often fever, rapid pulse and respirations, and enlargement of the

spleen, liver and regional lymph nodes. In addition to the subcutaneous hemorrhages, there is often an ulcerating stomatitis and evidence of bleeding from the nose, rectum and other mucous membranes. The marked anemia, thrombocytopenia and displacement of functional leucocytes by the proliferating primitive leucocytes account for most of the symptoms, such as pallor and dyspnea, rapid pulse, tendency to hemorrhage and infection. The invasion of the internal viscera and the hemapoietic organs by metastatic colonies of malignant leucocytes accounts for the enlargement of the liver, spleen and lymph nodes, and for the frequency of subcutaneous nodules or the tumor masses that involve the bones in the region of the orbit.

Laboratory Examinations: Examination of the peripheral blood was formerly considered conclusive for the diagnosis of leukemia, but with the recognition of subleukemic forms, this is no longer the case. Moreover, in severe infections in childhood, the white count may be as high as 100,000, with relatively large numbers of immature white blood cells in the peripheral blood. For this reason, studies of the sternal marrow or excised lymph nodes are often required for accurate diagnosis. Cases of leukemia in childhood with an extremely atypical onset are not rate. I have seen the disease begin with a solitary tumor in the soft parts of the forearm in a child of 10 months that had been diagnosed pathologically as "round cell sarcoma" following excision of the tumor. Since re-examination of the tissue failed to reveal the histologic architecture of fascial sarcoma, Ewing's sarcoma or neuroblastoma, a diagnosis of subleukemic myelogenous leukemia was ventured, and within 3 months the characteristic blood picture developed. This was in the days before puncture of the sternal marrow was used for diagnosis. In other cases, joint pains, suggesting rheumatic fever, characterize the onset and only the leukopenia and relative lymphocytosis suggest a contrary diagnosis. In such cases, x-rays of the long bones may reveal triangular defects in the bone behind the epiphysial line, which are characteristic of leukemia. Bone involvement with protuberant masses in the region of the orbit may be a presenting feature. This is also found in cases of neuroblastoma of the adrenal and the forms of leukemia known as chloroma. Splenomegaly and extreme pallor, which may be the initial findings in leukemia, are also found in congenital anemias, such as erythroblastosis fetalis, Mediterranean anemia and hemolytic icterus. In the anemias, however, there are blast forms of the erythropoietic series as well as those of the myelogenous series in the blood smear.

Definitive Diagnosis from Bone Marrow Studies: In lymphatic leukemia in children and adults, a definitive diagnosis cannot be based on the bone marrow, since this is not the organ primarily involved by the leukemic state. However, excision of the lymph node permits a positive diagnosis when the

picture is that of lymphosarcoma with obliteration of germinal centers, invasion of the capsule, and a crowding together of lymphoblasts of uniform size with dense nuclei and frequent mitotic figures. In myelogenous leukemia, an absolute diagnosis can be arrived at by adequate studies on material obtained from aspiration of the sternal marrow. In order to arrive at such a diagnosis, differential counts must be made from stained smears. A count of 2000 cells is made, in which the differing developing forms of the myelogenous series are recorded and the number of mitoses for both the myeloblasts and the promyelocytes. With this data, charts can be drawn showing the pattern of development in the marrow. In the normal bone marrow, the intermitotic forms among the myeloblasts and promyelocytes are practically constant, while in true leukemia, there is always an absolute increase in the number of intermitotic cells. In acute leukemia, this increase in intermitotic cells affects the myeloblasts; in chronic leukemia, it affects the promyelocytes; in the subacute form, both the myeloblasts and promyelocytes are affected.

Nature of the Leukemic Process: In the tabulation below, the distribution of cells in the various stages of development in normal and leukemic bone marrow is given. The proportion of cells shown is based upon the sampling of 2000 cells. The figures shown have been corrected to allow for the fact that the bone marrow is one-third diluted by peripheral blood. This correction must be made in calculating the distribution of cells in the normal marrow in the granulocytic series. Such a correction is not necessary in fully developed leukemia, where the bone marrow is in equilibrium with the peripheral blood, since all the forms circulate in leukemia.

In the accompanying illustrations contrasting the proliferation and maturation cycles of the normal granulocytes with myelogenous leukemia, the relative number of cells in each state are shown and the number of hours which each cell spends in that state has been calculated. In arriving at these calculations, there are several fundamental considerations. First, the number of dividing cells per thousand must be known and the time spent in an individual mitosis must be calculated. Most biologists are agreed that the time spent in the mitosis that can be seen in the stained smear is one hour. Since in the normal bone marrow there are $2\frac{1}{2}$ cells per 1000 in mitoses, the time required for the tissue to completely renew itself would be 1000 hours divided by $2\frac{1}{2}$ or 400 hours. This cycle must be divided into two phases; the first is the intermitotic cycle in which the cells take no part in development but remain behind as undifferentiated forms to divide again. The other is the maturation cycle in which the blast forms gradually mature to become promyelocytes, myelocytes and segmented forms. Under the microscope, it is impossible to tell an intermitotic myeloblast

which is waiting to divide again from a resting myeloblast which is waiting to mature and to differentiate into a fully-developed segmented leucocyte. In making the bone marrow counts, it is assumed that one-half of the myeloblasts are intermitotics and one-half are resting cells awaiting maturation. The same is assumed for the promyelocytes. This assumption is not arbitrary but rests upon a sound basis. When a blast cell divides, if both

TABLE 1

CELLS	NORMAL	CHRONIC MYELOID LEUKEMIA	ACUTE MYELOID LEUKEMIA
Dividing Cells:			
Blasts	44 (22 intermitotics; 22 resting) 10 hours	16 (8 I; 8 R) 2 hours	1510 (1210 I; 300 R) 30 hours
Promyelocytes	110 (55 intermitotics; 55 resting) 5 hours	160 (64 I; 96 R) 12 hours	300 30 hours
Maturing Cells:			
Myelocytes	308 60 hours	520 62 hours	50 5 hours
Juvenile leucocytes	388 78 hours	390 47 hours	50 5 hours
Band leucocytes	388 45 hours	330 40 hours	15 1.5 hours
Mature Cells:			
Segmented leucocytes	940 190 hours	550 64 hours	75 8.5 hours
Total time of cycle:	400 hours	250 hours	230 hours

daughter cells mature and lose the power of division, the tissue soon would be unable to renew itself. If both halves of the dividing cell, instead, remain behind to divide again, the number of intermitotic cells would rapidly increase and with degeneration of mature forms there would be inadequate replacement, followed by a fall in the cell count in the peripheral blood. Since the differential bone marrow count and the differential count of the peripheral blood in normal individuals is more or less a constant, in the final

analysis, this constancy can only be maintained when one of the pair of recently divided cells remains behind as an intermitotic form to divide

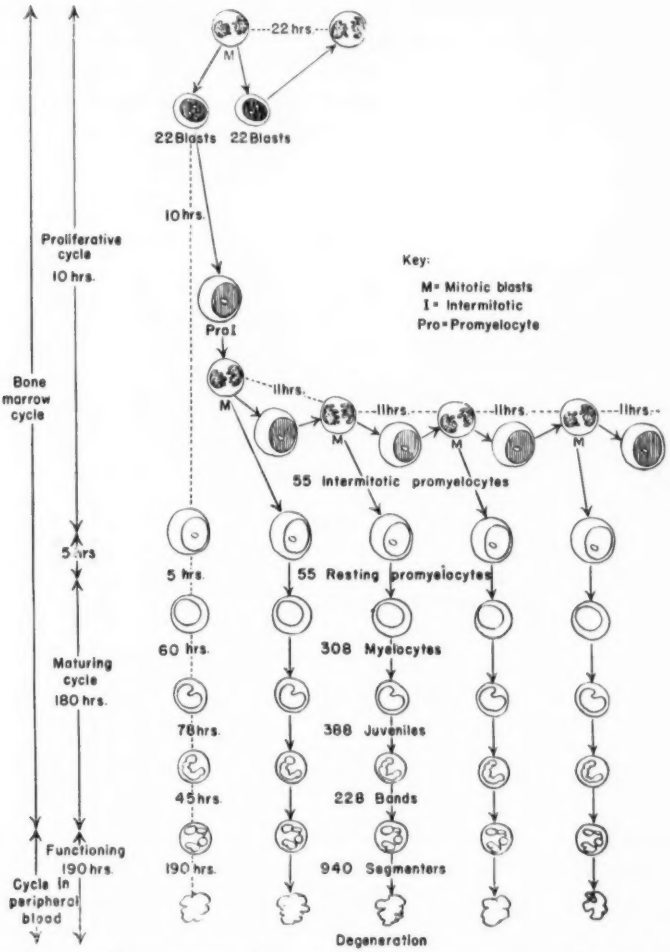

FIG. 1. NORMAL NEUTROPHILIC GRANULOCYTES PROLIFERATION AND MATURATION CYCLE (400 HRS.)

again, while the other matures to supply additional replacements for the colony of functioning cells.

With these considerations in mind, the graph shown in figure 1 was drawn.

It will be seen that in the normal bone marrow there are 22 intermitotic blasts per 2000 cells, or 11 per 1000. There are 55 intermitotic promyelocytes per 2000 or 22.5 per 1000. The interval between mitosis is 22 hours for the myeloblast and 11 hours for the promyelocyte. Since the number of cells in the different developmental stages is proportional to the time that each spends in that stage, it can be calculated that 190 hours is spent by a cell in passing from the myeloblast to the adult segmented form, or roughly 200 hours or 8 days. By actual count, a similar time, or 8 days, is spent by

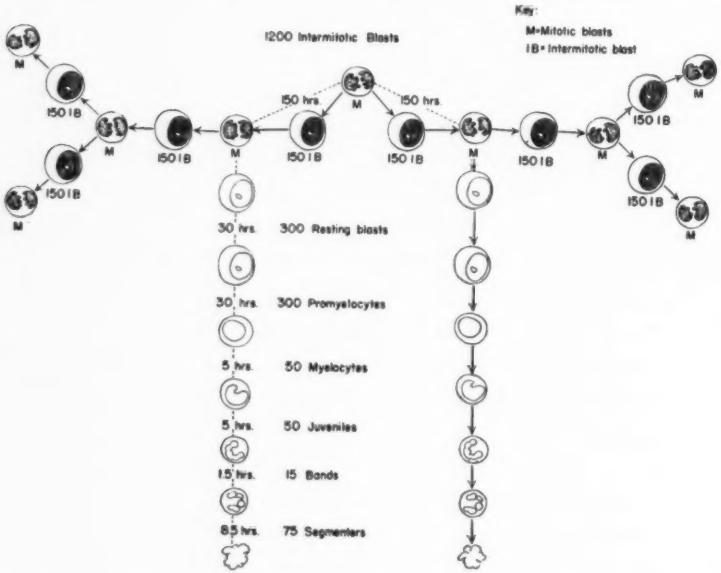

FIG. 2. ACUTE MYELOGENOUS LEUKEMIA PROLIFERATION AND MATURATION CYCLE (230 HRS.)

the adult granulocyte in the circulating blood. It was not known in advance that these two periods (8 days spent in development and 8 days spent in the circulation in the mature form) would equal each other. Obviously, however, if they did not the peripheral count could not remain at a constant level nor could the bone marrow count be maintained. This is evidence in favor of the correctness of the calculations made. It can be seen from the representative graph made of acute myelogenous leukemia (figure 2) that in every other generation following cell division both cells remain behind as intermitotics and divide again, without attempting maturation. Thus,

there is a marked increase in the number of intermitotic blast forms which number 1200 out of 2000, or 60%. (The normal is only 11 per 1000 or 1%.) With such an overabundance of regenerating cells among the myeloblasts, division in the promyelocytes is unnecessary and is therefore inhibited. The promyelocytes also spend a longer time in differentiating, their resting stage increasing from 5 to 30 hours.

In chronic myelogenous leukemia (figure 3), the increase among the inter-

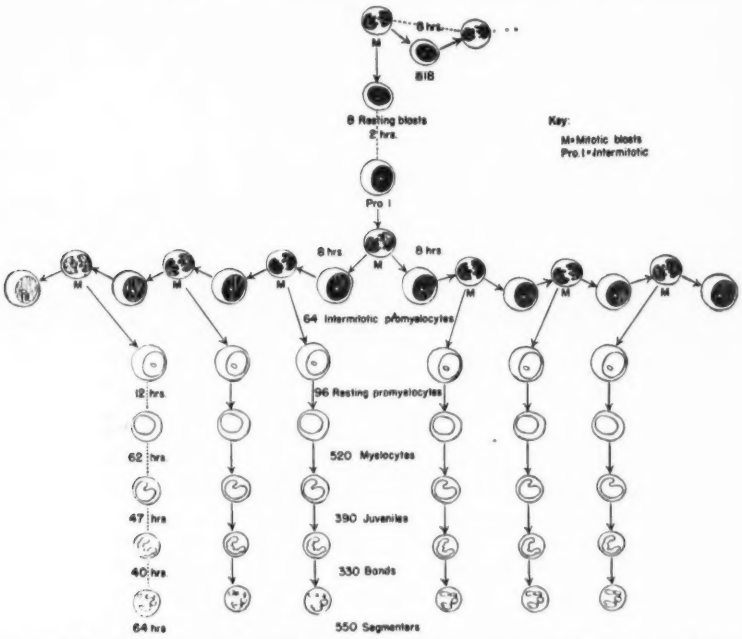

FIG. 3. CHRONIC MYELOGENOUS LEUKEMIA PROLIFERATION AND MATURATION CYCLE (250 HRS.)

mitotic colony affects the promyelocytes, which are increased from 55 to 64 per 2000, in the case shown. Again, the number of resting promyelocytes is increased and their time spent in maturation is increased from 5 to 12 hours. The maturation arrest in the promyelocytes in chronic myelogenous leukemia does not relieve the myeloblastic cells of their function of proliferation. The affect is apparently the opposite, since the blast forms divide more rapidly (the intermitotic time is reduced from 22 to 8 hours) and the resting forms spend only 2 instead of 10 hours in passing from the myeloblasts to the promyelocyte stage.

These graphs on leukemia demonstrate the disease to be a truly malignant neoplasm, since a similar maturation arrest with increase in the intermitotic cells has been demonstrated for other forms of malignancy. Gluckman has found a similar increase in the intermitotic count among the epidermal cells of the skin in the development of epidermal carcinoma in mice painted with benzpyrene.

Treatment of Leukemia: In leukemia, the major form of therapy has been radiant energy. Irradiation to the spleen or to the red marrow bones can be used in the chronic forms to lower the total count and to reduce the mass of neoplastic tissue. As a refinement in radiation therapy, radioactive phosphorus produced in the cyclotron has been given both orally and parenterally. This substance is deposited in greatest concentration in bone

TABLE 2

Table showing the average number of cells in varying stages of development in untreated and benzpyrene painted mouse epidermis in mice developing skin cancer

GROUP	DIFFERENTIATING	DEGENERATE	INTERMITOTIC OR RESTING	MITOTIC	RESTING CELLS IN MITOSIS
1. Adult Controls	92	5	16	1.3	8
2. 0–24 hrs. after single benzpyrene painting	99	10	25	3	12
3. 2–7 days after single benzpyrene painting	137	12	49	5	10
4. 8–49 days after repeated benzpyrene paintings	142	21	53	6	11
5. Papillomatous regions, 63–70 days after repeated paintings	148	28	143	9	6
6. Carcinomatous regions, 74–119 days after repeated paintings	83	17	132	10	8

marrow, liver, spleen and lymph nodes and thus release its radioactivity in the tissues where the leukemic cells are most numerous. Unfortunately this radioactivity also injures the erythopoietic tissues and cannot be used where repeated transfusions fail to maintain the red cell count. Other experimental forms of therapy, such as mustard gas, and colchicine, which depress the white count, have proved relatively ineffective because of the severe anemia and thrombocytopenia. The only treatment is repeated transfusion to relieve the profound anemia and tendency to hemorrhage. Irradiation of an enlarged spleen may be given for symptomatic relief.

Because of the inadequacy of all forms of therapy, the author has experimented with a certain dye substance and oil-soluble compounds containing heavy metal radicals, because experiments have shown that these sub-

stances, like radioactive phosphorus, are selectively deposited in the marrow, the liver, spleen and lymph nodes. Before using any of these substances, however, they were all tried on normal animals and any of them which caused a depression of the normal white or red cell count were discarded. What was desired was an injectable substance selectively absorbed by the erythropoietic tissues which would not prove harmful to the normal cells of these tissues, but which might selectively damage the immature leukemic forms. As a result of these experiments, an oil-soluble copper compound was selected which was found to depress the white cell count in chronic, subacute and acute myelogenous leukemia. It is too early to report the influence of this compound on the subsequent clinical course of the disease, nor can it be stated that any permanent cure can be affected. Encouraging results, however, have been obtained in as much as the total leukemic count can be readily reduced by a non-toxic substance with a corresponding rise in the erythrocytes and clinical improvement of the patient's condition. When the substance is given in amounts totaling 100 to 250 mgs. over a period of a week or so there is, in addition to the lowering of the white cell count, a rapid regression in the size of the spleen and in the size of the palpable enlarged liver or lymph nodes.

CYSTIC DISEASE OF THE LUNG

Case Report No. 67

Dr. Robert L. Simpson J. W.—46–5127

J. W., a 7 year old white girl, was admitted to this hospital on June 11, 1946 because of shortness of breath and cyanosis of three days' duration, which symptoms had appeared during her convalescence from an attack of measles. The measles had had its onset with a rash on June 2, 1946, accompanied by cough and fever. Following the subsidence of the fever the cough had persisted until her admission. On June 8 she complained of pains in her chest and the next day developed progressively increasing dyspnea accompanied by cyanosis of the face and hands.

The child had been born at home in rural Maryland after a full term normal delivery and her early development and feeding history were normal. At the age of 3 years she contracted whooping cough as did her brother and sister and apparently made an uneventful recovery from this illness. According to her mother the child appeared perfectly normal and exercised to the same degree as her playmates without exhibiting any manifestations of fatigue, shortness of breath or cyanosis. A physician examined her in September, 1945 upon her entrance into school and she was said to be perfectly normal at that time.

Physical examination upon admission revealed a well developed, poorly nourished and somewhat dehydrated white female child who appeared critically ill. She was markedly orthopneic and there was cyanosis of the lips, fingers and toes. There was dulness upon percussion and tubular breathing over the left upper lobe anteriorly and the entire right lung exhibited medium and coarse moist inspiratory rales throughout. A pleural friction rub was elicited over the left lower lobe in the axillary line. The heart sounds were distant and the rhythm was irregular. The abdomen was flat and soft and the liver edge was barely palpable. There was a grade 1 pitting edema of the ankles and marked clubbing and cyanosis of the fingers and toes. Her skin was dry and granular to touch with a barely discernible brownish-red macular papular rash.

Blood counts and urinalyses were essentially normal and a venous pressure estimation made on the second day after admission was 300 mm. of normal saline. Her temperature ranged between 100° and 102°; pulse between 100 and 160; respirations between 30 and 64. The electrocardiogram revealed a sinus tachycardia at the rate of 155, P.R. interval of 0.12 and some right axis deviation with an inverted T 3: Interpretation, right ventricular hypertrophy and strain.

The child was given 50,000 units of penicillin intramuscularly as an initial dose, followed by 40,000 units every 3 hours. Sulfadiazine was administered orally in full doses on the basis of 1½ grains per pound of body weight. She was digitalized by the administration of 4 C.U. of digifoline over a period of 48 hours, and was maintained on ½ cat unit per day until the subsidence of symptoms and signs of congestive failure. An oxygen tent was employed continuously with the patient in an upright position until the 8th

FIG. 1. ILLUSTRATING CLUBBED FINGERS AND TOES ASSOCIATED WITH THIS CASE OF CYSTIC DISEASE OF THE LUNG

hospital day when she was able to breathe normally without its aid. During this period the dyspnea and cyanosis gradually disappeared, her pulse became normal as did her respirations and temperature.

Roentgenographic examination upon admission revealed a diffuse fuzzy infiltration throughout both lungs more marked on the left side with numerous cystic appearing shadows throughout both lungs but more marked on the left. The appearance was that of acquired cystic disease complicated by a superimposed pneumonic process. The heart shadow did not appear

to be enlarged. Follow-up x-rays of the chest during the next 4 weeks revealed the infiltrative lesions to resolve in the right lung but the cystic shadows in the left base persisted and resembled cystic bronchiectasis.

With the subsidence of the systemic symptoms during the first two weeks of her hospital stay her cough which was productive of a foul smelling green sputum gradually subsided except for small amounts which were still present four weeks later at the time of her discharge. The patient is to be observed closely for a period of three months at which time a lipiodal study of the

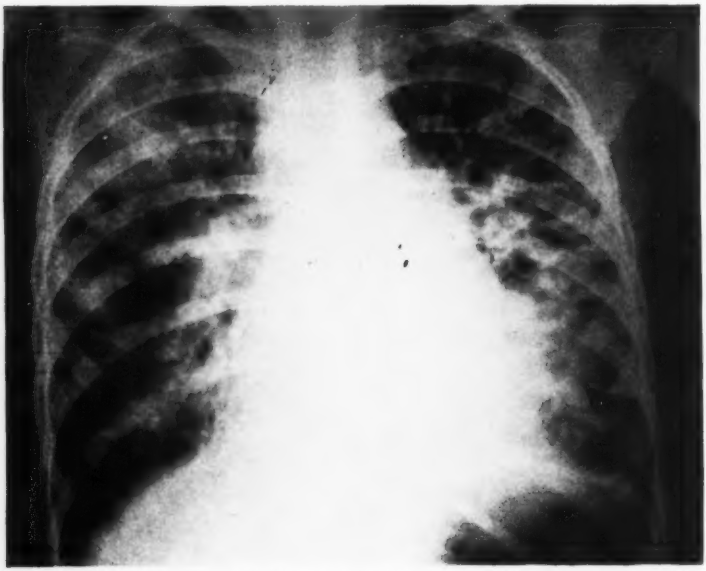

Fig. 2. Note the Cystic Appearing Areas Especially Throughout the Left Lung. This X-ray was Taken upon Admission

lung structure will be made with a view to surgery if the changes appear permanent and involve just the one lobe.

Discussion

Roy Klepser, M.D.

Any abnormality of the lung in which cysts or cyst-like structures are found, regardless of their pathogenesis, is usually called cystic disease. Used in this loose sense, it includes "cystic bronchiectasis" as well as bronchogenic cysts, pneumatoceles and emphysematous blebs or bullae. Cylindrical and saccular types of bronchiectasis are excluded from this terminology, as are tuberculous cavities and other specific infections.

Dickson, Clagett and McDonald[1], of the Mayo Clinic, have attempted to classify cystic disease by pathogenesis, and have tried to differentiate between the true developmental or congenital cysts and the acquired cysts. The latter group would include cystic bronchiectasis, pneumatoceles, abscess cavities and emphysematous dilatations. The actual nomenclature is often of academic interest only, surgical treatment being influenced by other factors which vary with each case. The extensiveness of the disease, as in the case just presented for example, may preclude surgical removal of the affected lobes, even though such surgical excision is known to be the only effective treatment for such disease.

The true developmental cysts, which are probably all congenital, although some do not become apparent by x-ray until later in life, are characterized by a uniform mucosal lining which is identical with bronchial epithelium. The surrounding structures, however, as described by Dickson, Clagett and McDonald[1] are very disordered. Mixed areas of muscle, elastic tissue, cartilage and glands are haphazardly scattered beneath the mucosa. This disarrangement is in contrast to that of the simply dilated bronchus of acquired cysts in which the arrangement remains orderly.

In comparing the developmental or congenital type of cyst with the acquired form of "cystic bronchiectasis," other factors are apparent. We often arbitrarily distinguish those cysts which are below 3 or 4 cm. in size in the x-ray as cystic bronchiectasis. Such cysts are most frequently in the basilar lobes of the lungs and in almost all cases the cystic areas can be shown to have direct bronchial communication when a bronchographic contrast medium is used. The cysts of a bronchiectatic process are usually centered about a bronchus, and are usually multiple. In the congenital form, the cyst may be in the mediastinum, connected to a bronchus by a process which may or may not be patent.

Operative treatment for cystic disease consists of removal of the involved portion of the lung.[2] Occasionally this can be done by local excision of the cyst or by segmental resection of a portion of a lobe. The acquired form, as cystic bronchiectasis, is more widespread, and it is seldom that less than one lobe need be removed. In the case just presented, the involvement is very widespread. It follows a bronchial arrangement and the cystic areas are smaller than 4 cm. in size. This is probably an acquired type of cystic bronchiectasis. The diffuse pattern of distribution in this case, involving several lobes of each side, makes excision impractical, for too many lobes seem to be involved. No other type of surgery, such as drainage or collapsing operations, has proven effective in these cases.

BIBLIOGRAPHY

(1) Dickson, J. A., Clagett, O. T. and McDonald, J. R.: Cystic disease of the lungs and its relationship to bronchiectatic cavities. J. Thoracic Surg. **15:** 196, 1946.

(2) Maier, H. C.: Surgical treatment of bronchiectasis. Surgery. **15:** 789, 1944.

VERTEBRAL FRACTURE ASSOCIATED WITH INTRASPINAL INJURY IN THE NEWBORN

Case Report No. 68

Dr. Clifford J. Tichenor

M. T., a thirty-four year old colored primi para, was brought to the delivery room of a local hospital at term, in active labor, the fetus being ostensibly alive and normally active. The presentation was a right sacral anterior; immediate complications were a prolapsed cord and a borderline pelvic inlet, the diagonal conjugate barely measuring 11 cm. Breech extraction was performed, with Piper forceps applied to the aftercoming head. The head and shoulders were peculiarly hard to deliver and required a great deal of traction. At one point the hyperextension used was sufficient to bring the infant's lower extremities up on to the maternal anterior abdominal wall. At this time a distinct crunching sound was audible and some bone or joint injury was suspected.

Immediately after birth, resuscitative measures were begun. The skin color was purplish-red and all extremities were flaccid. The limpid, atonic infant did not cry or make any attempt to breathe. The pupils were equal but fixed in mid-dilatation and did not react to light. By using the Kreiselman model Heidbrink resuscitator for delivering oxygen under low controlled pressure into the posterior nasopharynx, a shallow, irregular breathing became visible in the uppermost anterior chest. There was no apparent intercostal, diaphragmatic or abdominal contractions.

The heart beat was strong, regular, and slow. The Moro embrace reflex was entirely absent. Sucking and swallowing reflexes were present. The skin became moderately cool and no cutaneous irritability could be demonstrated. Since the cry was not forthcoming and respirations were extremely shallow and irregular, and pure oxygen was not sufficient in the active treatment of the asphyxia, a mixture of 7% carbon dioxide and oxygen was administered, but without success. The skin became pallorous and cyanosis manifested itself primarily in the lips.

At this time, one hour after delivery, a more complete examination of the newborn revealed an abnormal lateral mobility of the mid-dorsal spinal column. Birth trauma, involving fracture of dislocation of the thoracic vertebrae and possible intracranial injury was postulated. In spite of continuous resuscitative measures, the infant expired at the end of three hours.

Post-mortem x-rays of the skull and spinal column were done. Roentgenological examination of the cranium was normal but the dorsal spine was remarkable at the 5–6 thoracic level. This is well illustrated in the accompanying photograph.

FIG. 1

FIG. 2

Necropsy revealed a complete separation of the 5–6 T with torsion and narrowing of the cord. There was a massive hemorrhage into the posterior mediastinum from traumatic laceration of the vertebral vessels. There was also a complete fracture of the body of 6 C. Examination of the intracranial cavity demonstrated a large rupture of the falx cerebri at the anterior fontanelle and gross hemorrhage over the entire brain stem.

Discussion

Fractures and dislocations of the vertebrae are rare and are usually the result of difficulty in delivering the after-coming head. The symptoms depend upon the site of fracture and the extent of compression of the cord or of injury to the roots of the peripheral nerves. The prognosis is grave. The seat of the fracture is most often the body of the sixth cervical vertebra, the body of the vertebra being weaker than the connection between the disk and the body. The result of this fracture is nearly always death and the injuries are nearly always accompanied by hemorrhage into the spinal canal.

Except for those natal disturbances associated with anoxia most birth injuries are related to traumatic factors operative in labor or at delivery. Almost any structure in the body can be involved and include fractures, dislocations, hemorrhage, nerve injuries and injury to the soft parts.

One of the commonest fractures is that of the clavicle, especially when there is difficulty in delivery of a shoulder. Characteristically the infant fails to freely move the affected side and the Moro reflex is unilaterally absent. Humeral fractures and brachial palsy may also be responsible for such limitation so that x-ray is invaluable in the differential diagnosis. The immobilization of the arm and shoulder is an orthopedic problem. Callous formation is remarkable within a week and the prognosis is excellent with early diagnosis and treatment.

Fractures of the long bones of the arms and legs may occur if there is difficulty in delivery an extremity. Usually the fracture site can be easily palpated. Spontaneous movement of the part is absent and the Moro reflex is asymmetrical. The possibility of associated nerve involvement must always be considered.

Skull fractures are uncommon, but when they do occur are apt to be associated with intracranial hemorrhage and the prognosis is grave.

When traction is exerted on the head without freeing the shoulder, injury may result to the nerve fibers of the brachial plexus, causing a paralysis of the upper arm with or without a paralysis of the forearm or hand. When the injury is limited to the 5th and 6th cervical roots or their trunks, there is loss of ability to abduct the arm from the shoulder, to rotate the arm externally, and to supinate the forearm. The biceps reflex is absent and the Moro reflex is absent on the affected side. This condition is classically

described as Erb's paralysis. Unless the lower portion of the plexus is involved, the power of the forearm and hand will be retained.

The rare Klumpke's paralysis involves injury to the seventh and eighth cervical and the first thoracic nerves or their trunks and results in a paralyzed hand. Ptosis and miosis also appear when the sympathetic fibers of the first thoracic root are traumatized.

Facial paralysis of the peripheral type sometimes results from direct pressure over the facial nerve by forceps during delivery. This can be readily recognized when the infant cries, as there is movement on only one side of the face and the mouth is drawn to that side. The eye stays open on the affected side.

Subperiosteal collections of blood on the scalp, or cephalohematomas, may occur from maternal pelvic friction or forceps application and are limited to the surface of one cranial bone.

The sternocleidomastoid muscle may be injured during delivery, especially breech extractions, and is characterized by swelling in the mid-portion of the belly of the muscle, usually seen in the second week of life and causing a torticollis.

The clear-cut demarcations of intracranial hemorrhage are seldom seen, but such a condition should be suspected when there is undue apathy and somnolence, restlessness, pallor, cyanotic attacks, poor sucking reflex, high pitched shrill cry, muscular twitchings or frank convulsions, paralysis, irregular weak breathing, absent Moro reflex—especially when there is a history of maternal-fetal disproportion, prolonged labor or mechanical interference at delivery.

In conclusion, breech presentations may result in massive adrenal hemorrhage, the result of direct trauma to the renal areas and causing the infant to be stillborn or to die shortly after birth in profound shock.

Thus it becomes apparent that disturbances related to birth may cause temporary effects or produce permanent damage and not uncommonly death. In this paper some of the more frequent conditions which arise as a result of trauma at birth have been briefly discussed. A rare case of vertebral fracture was presented.

CLINICO-PATHOLOGICAL CONFERENCE

Directed by Dr. E. Clarence Rice
Assisted by Dr. Lois Murphy

Case Report No. 69

Dr. Lois Murphy V. W.—42-1191

V. W., a 4 year old white girl, was admitted to the Children's Hospital because of an enlarged abdomen. The mother had noticed the abdominal enlargement only a few days preceding admission and believed the mass was becoming progressively larger each day. At the time the tumor was discovered, the child began to have occasional vomiting and she developed an associated urinary frequency. There was no constipation, dysuria, vaginal discharge or history of trauma.

The child was born one month prematurely and the birth weight was 5 lbs. 10 oz. The delivery was spontaneous. She was breast fed for nine months. The only previous illnesses were pertussis at nine months and measles at three years. She received immunizations for diphtheria and smallpox. The family history was non-contributory.

On physical examination the patient was a well developed, slender colored girl who did not appear actuely ill. The only positive finding was a large, firm abdominal mass which was visible on inspection and readily palpated (figure 1). It extended like a large, inverted pear from the pubic bone to the umbilicus and was not freely movable. The patient complained of pain when the mass was palpated. The external genitalia and urethral orifice were edematous. Rectal examination showed the adnexa to be normal. There were no secondary sex changes and no lymphadenopathy was found. Her temperature on admission was 101°, pulse rate 105 and respiratory rate 25 per minute.

Hemogram revealed a hemoglobin of 10.5 gms. and the white cell count was 7000 with 50% neutrophils. Urine examination on 3 different occasions was negative.

Roentgenographic examination revealed a dense mass arising from the pelvis and extending into the abdomen to about the level of the 4th lumbar vertebra. A barium enema showed the sigmoid and distal portion of the descending colon to be displaced upwards and towards the right by the tumor mass in the midline. An intravenous and retrograde pyelogram failed to reveal any abnormality.

A laporotomy was performed 3 days after admission. There was found a degenerative solid tumor arising from the right ovary. The degenerative process had involved the mesentery of the small bowel over a small area

but there was no extension into the broad ligament. The degenerative material appeared granular and white. All of the tumor mass could not be removed. The liver and left ovary were normal.

The postoperative course was uneventful. The temperature became

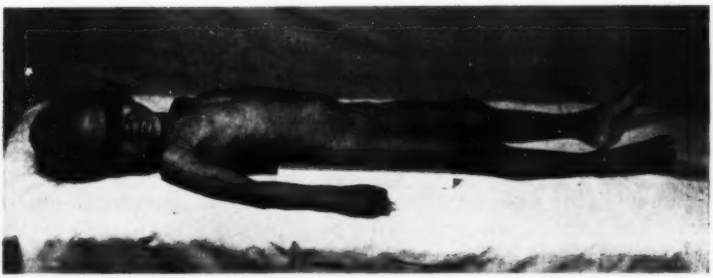

FIG. 1. NOTE ABDOMINAL MASS EXTENDING FROM UMBILICUS TO SUPRAPUBIC REGION

FIG. 2.

normal within 2 days and the child appeared moderately well. Supportive therapy included 500 cc. of blood and 200 cc. of plasma. She was discharged on the twentieth postoperative day.

On gross examination the tumor weighed 135 grams and measured 14 ×

7 × 5 centimeters (figure 2). One surface was enclosed by a fibrous capsule and the other was degenerated, hemorrhagic and irregular with no capsule present.

The microscopic examination revealed two rather definite types of tissue in different portions of the tumor: (1) Tissue of mesothelial type was found in irregular plaques, mingled with relatively large areas of degenerated and necrotic material. Well defined vascular spaces were noted. In many areas the cells were vacuolated suggesting fat. Some groups of endothelial cells were also seen. In general the structure was made up of small endothelial lined spaces with a considerable portion being vascular; (2) The other type of tissue had structures similar to those described above with large vascular spaces filled with red cells and large plaques of fat-like tissue. There were in this section many epithelial lined spaces varying in size and outline from small lumina surrounded by a uniform layer of cuboidal cells having the appearance of a duct, to larger branching glandular formations. Frequently there were plaques of cells representing broadening or thickening of the walls of both mesothelial and epithelial structures. These histological sections were thought to be compatible with a diagnosis of teratoma of the ovary which was in all probability malignant.

Discussion

One of the common sites of neoplasm in childhood is the ovary, and this frequently becomes more evident with the onset of puberty. Sixty per cent of cysts and tumors of the ovary are malignant. Teratomas are more common than sarcomas and carcinomas and the prognosis is more favorable with teratoma than sarcoma or carcinoma.

Teratomas are composed of structures derived from more than one of the three embryonic tissues, ectoderm, endoderm and mesoderm. There are two types of this tumor which are commonly recognized. One is the solid teratoma and the other the cystic dermoid. They are considered by Ewing[1] to represent the embryonic and adult types of the same growth. Barzilai[2] distinguishes an embryonal type which shows less organoid differentiation. Clinically this type metastasizes more readily and is found in younger individuals. This type, if malignant from the onset, may reach considerable size and it characteristically becomes adherent to surrounding structures. The tumor may become attached to abdominal organs. Distant metastases occur later and postoperative recurrence is usual.

In children the size of the tumor need not necessarily predicate its malignant character. Ladd and Gross[3] state that surgical excision may be followed by chances for permanent cure and do not generally recommend postoperative irradiation as desirable since it is followed by inevitable sterilization. At the same time, the malignant cells, if left after operation,

may not be destroyed by x-ray therapy. Barzilai[2], however, recommends irradiation.

REFERENCES:

1. Ewing, J.: Neoplastic Diseases. W. B. Saunders: Philadelphia. 4th edition, 1941.
2. Barzalai, G.: Atlas of Ovarian Tumors, Grune and Stratton: New York, 1943.
3. Ladd, W. E. and Gross, R. E.: Abdominal Surgery of Infants and Children. W. B. Saunders: Philadelphia, 1941.
4. Foot, N. C.: Pathology in Surgery. J. B. Lippincott: Philadelphia, 1945.
5. Brenneman: Practice of Pediatrics.